Phillipe Lucas, MA, PhD(c)

Philippe Lucas is Vice President, Global Patient Research & Access at Tilray and a Graduate Scholar with the Centre for Addictions Research of British Columbia. His scientific research and publications include studies on the therapeutic use of cannabis, with a focus on the treatment of trauma and addiction. Philippe has provided expert testimony before the Canadian House of Commons and Senate and the BC Supreme Court, and in 2013 he was awarded the Queen Elizabeth II Diamond Jubilee Medal for his work and research on medical cannabis.

RESEARCH CORNER: CANNABIS IN THE TREATMENT OF HEADACHES, MIGRAINES, AND ANXIETY, AND IT'S IMPACT ON OPIOID AND PRESCRIPTION SUBSTANCE USE

Nothing teaches patience quite like conducting human health research. Research on individuals demands determination, attention to detail, and humility, with the outcome of all that planning, and perseverance not being known for weeks, months, or years, depending on the study design.

In the best of cases, research is a labour of love, with the reward not being monetary, nor typically taking the form of awards or prizes. More often than not, the modest outcome is the publication of results in a peer-reviewed journal and an acknowledgement from a few fellow academics that all that hard work was not for naught. Sometimes the world notices and perhaps even changes. Much of the time a new reference is added to a PubMed search and the world goes on.

Regardless of the impact, academics do this formal dance because we understand and accept this is how new scientific knowledge is formed; not with rare and dramatic eureka moments, but with the slow stacking of evidence on a scale that delicately balances one way or the other. Science is rarely absolute, but an honest and earnest debate of ideas, and of ways to challenge the same via research and the publication of findings.

In this article, it's my pleasure to present triplets born of this laboured academic process: 3 new publications stemming from the Tilray Patient Survey 2017 (TPS17). They are the result of collaborations between Tilray and academics across Canada and the US, and their findings, while limited, may add to our understanding of the impact of medical cannabis on pain and headaches, anxiety, and the use of opioids and other substances. The Tilray Patient Survey 2017 is a 239-question instrument distributed online in January 2017 to authorized medical cannabis patients across Canada, ultimately gathering 2,032 complete responses. The study included a number of academic collaborations, including the contribution of validated questions specific to headaches and migraines by neurologist Dr. Eric Baron from Cleveland Clinic, as well as instruments specific to anxiety by Dr. Michael Van Ameringen from McMaster University.

The first article is titled Patterns of medicinal cannabis use, strain analysis, and substitution effect among patients with migraine, headache, arthritis, and chronic pain in a medicinal cannabis cohort and was published in the Journal of Headache and Pain.[1] Baron provided the ID Migraine™ questionnaire, a validated instrument used to predict the probability of migraine in patients. Patients who self-identified as migraine or headache sufferers filled out the questionnaire, and then were compared with the general patient population to identify patterns of use specific to this sub-population. Overall, 505 patients (24.9%) identified headaches as a symptom for which they used cannabis, with 75 citing it as a primary condition. Based on the analysis of the ID Migraine™, 88% (n = 445) of headache patients were

treating probable migraine with cannabis. Prescription substitution in headache patients included opiates/opioids (43.4%), antidepressants/anti-anxiety medications (39%), nonsteroidal anti-inflammatories (21%), triptans (8.1%), anticonvulsants (7.7%), and muscle relaxers (7%).

Perhaps the most interesting finding of the study came from a sub-analysis of the strain preferences identified by this patient population. Hybrid strains were preferred by headache sufferers, as well as most pain groups, with OG Shark, a high tetrahydrocannabinol (THC)/low cannabidiol (CBD) strain with predominant terpenes β-caryophyllene and β-myrcene, most preferred in the headache and ID Migraine™ groups. The researchers suggest this could be due to the analgesic, anti-inflammatory, and antiemetic properties of THC, coupled with the known anti-inflammatory and analgesic properties of β-caryophyllene and β-myrcene. To the best of my knowledge, this is the first time a specific strain and associated terpene and cannabinoid profile has been statistically identified with the treatment of a primary condition like headache/migraine/pain, and this could point the way to more specific cannabis-based treatments for these conditions in the future. There appears to be keen interest in this, as the article is amongst the top 10 most popular at this journal with over 9,000 accesses to date!

The second article is titled Cannabis use behaviors and prevalence of anxiety and depressive symptoms in a cohort of Canadian medicinal cannabis users, and was published in the Journal of Psychiatric Research.[2] Prof. Michael Van Ameringen, from McMaster University, provided a few validated instruments used to assess for anxiety/anxiety disorders; namely, the Generalized Anxiety Disorder 7-item, Patient Health Questionnaire-9, Mini-Social Phobia Inventory, and panic disorder/agoraphobia Diagnostic and Statistical Manual of Mental Disorders criteria. Findings from these instruments showed that the prevalence rate of anxiety in this population was very high. Overall, 43.7% (n = 888) of this population cited anxiety as a symptom which they treated with cannabis, and 63.4% met screening criteria for ≥1 disorders: 45.6% potentially qualifying for generalized anxiety disorder, 42.4% for social anxiety disorder, 25.7% for major depressive disorder, and 25.7% for panic disorder/agoraphobia.

THE FINDINGS SUGGEST THAT MOST OF THESE PATIENTS FOUND CANNABIS HELPFUL IN TREATING THEIR ANXIETY, WITH 92% REPORTING IT IMPROVED THEIR SYMPTOMS

despite continuing to report symptoms of moderate-level severity. In fact, greater cannabis use was associated with higher symptom severity, suggesting that either increased symptoms led to greater use, or that despite higher rates of use, symptoms persisted.

Nearly half (49%) of respondents reported using cannabis as a substitute for a nonpsychiatric (53.7%) or psychiatric medication (46.3%) (see Table 1). Although there's been much interest in the use of CBD in the treatment of anxiety and other mental health issues, high THC strains were most often rated as anxiolytic by this patient population.

Table 1. Proportion of the ANX Sample Replacing a Prescribed Medication with Medicinal Cannabis (n = 888).

Drug Class	%
Antidepressants	23.8
Opioid	19.2
Benzodiazepine	15.8
NSAIDs	6.1
Antiepileptic	5.0
Sedative-hypnotic	4.2
General analgesic	3.9
Psychostimulant	3.7
Antipsychotic	3.0
All others	15.3

NSAIDs=nonsteroidal anti-inflammatories

In light of the high percentage of patients citing the use of medical cannabis in the treatment of anxiety and mental health issues, and ongoing questions in regard to both the positive and negative impacts of THC and CBD on psychiatric disorders, more rigorous research in this therapeutic area is clearly justified.

The third paper stemming from the TPS17 is titled Medical cannabis patterns of use and substitution for opioids & other pharmaceutical drugs, alcohol, tobacco, and illicit substances; results from a cross-sectional survey of authorized patients, and was published in the Harm Reduction Journal.[3] Overall, pain and mental health conditions accounted for 83.7% of all respondents (n = 1,700), and researchers found a very high rate of self-reported substitution for prescription drugs (69.1%, n = 953), as well as alcohol (44.5%, n = 515), tobacco (31.1%, n = 406), and illicit substances (26.6%, n = 136). Opioid medications accounted for 35.3% of all prescription drug substitution (n = 610), followed by antidepressants (21.5%, n = 371) (see Table 2). Perhaps of most significance to public health, of the 610 mentions of specific opioid medications, patients report total cessation of use of opioid medication in 59.3% (n=362) of cases.

Table 2. Breakdown of Drugs Substituted with Cannabis Prescription Drugs

	(n, %)
1. Opiates/opioids	610; 35.3%
2. Anti-depressant/anti-anxiety	371; 21.5%
3. Non-opioid pain medications	189; 10.9%
4. Anti-seizure medications	149; 8.6%
5. Muscle relaxant/sleep aids	140; 8.1%
6. Benzodiazepines	75; 4.3%
7. Stimulants	59; 3.4%
8. Antiemetics	24; 1.4%
9. Antipsychotics	18; 1%

These results support other recent publications suggesting that cannabis can reduce the use of – and associated harms associated with – more dangerous substances such as alcohol, tobacco, opioids, and illicit substances, potentially resulting in improved patient outcomes and overall public health.[4-7] Encouragingly, the article has been accessed nearly 3,000 times, so perhaps some of these findings will ultimately find their way into public policy to address the ongoing opioid overdose crisis.

While there is still so much to learn about the therapeutic potential of cannabis, through ongoing collaborations on innovative observational and clinical studies, patients, academics, and healthcare providers are slowly and diligently filling the gaps of knowledge. The progress is long, slow, and systematic, but it is progress, nonetheless. We now know more about medical cannabis today than we did yesterday, and there is no doubt we'll know still more tomorrow.

REFERENCES:

1. Baron EP, Lucas P, Eades J, Hogue O. Patterns of medicinal cannabis use, strain analysis, and substitution effect among patients with migraine, headache, arthritis, and chronic pain in a medicinal cannabis cohort. J Headache Pain. 2018;19(1):37. doi.org/10.1186/s10194-018-0862-2.
2. Turna J, Simpson W, Patterson B, Lucas P, Van Ameringen M. Cannabis use behaviors and prevalence of anxiety and depressive symptoms in a cohort of Canadian medicinal cannabis users. J Psychiatr Res. 2019;(111):134-139. doi.org/10.1016/J.JPSYCHIRES.2019.01.024.
3. Lucas P, Baron E P, Jikomes N. Medical cannabis patterns of use and substitution for opioids & other pharmaceutical drugs, alcohol, tobacco, and illicit substances; results from a cross-sectional survey of authorized patients. Harm Reduct J. 2019;(16):9. doi.org/10.1186/s12954-019-0278-6.
4. Boehnke KF, Scott JR, Litinas E, Sisley S, Williams DA, Clauw DJ. Pills to pot: observational analyses of cannabis substitution among medical cannabis users with chronic pain. J Pain. 2019; pii: S1526-5900(18)30735-1. doi.org/10.1016/J.JPAIN.2019.01.010.
5. Santaella-Tenorio J, Mauro CM, Wall M, et al. US traffic fatalities, 1985-2014, and their relationship to medical marijuana laws. Am J Public Health. 2017;107(2):336-342. doi.org/10.2105/AJPH.2016.303577.
6. Socías ME, Kerr T, Wood E, et al. Intentional cannabis use to reduce crack cocaine use in a Canadian setting: A longitudinal analysis. Addict Behav. 2017;72:138-143. doi.org/10.1016/j.addbeh.2017.04.006.
7. Wen H, Hockenberry JM. Association of medical and adult-use marijuana laws with opioid prescribing for Medicaid enrollees. JAMA Intern Med. 2018; 178(5):673-679. doi.org/10.1001/jamainternmed.2018.1007.